In the United States Court of Federal Claims

LAURA KALAJDZIC and BOJAN KALAJDZIC on behalf of A.K., a minor child,

Petitioners,

v.

SECRETARY OF HEALTH AND HUMAN SERVICES,

Respondent.

No. 17-792V
(Filed: October 18, 2024)[1]

Amber Diane Wilson, Washington, DC, for Petitioners.

Claudia Barnes Gangi, Civil Division, United States Department of Justice, Washington, DC, for Respondent.

OPINION AND ORDER

LERNER, *Judge*.

Pending before the Court is Mr. and Mrs. Kalajdzic's ("Petitioners") Motion for Review of the Chief Special Master's Decision ("Dec.") denying them compensation under the National Childhood Vaccine Injury Act of 1986, 42 U.S.C. §§ 300aa-1 to -34 ("the Vaccine Act"). Petitioners argue that the FluMist influenza vaccine caused their son to develop narcolepsy with cataplexy. The Chief Special Master found that Petitioners failed to prove their claim by a preponderance of the evidence. In Petitioners' Motion for Review, they assert the Chief Special Master's decision was not in accordance with law. While the Court is not unsympathetic to the Kalajdzics' difficult struggle with narcolepsy, for the reasons set forth below, the Motion for Review is **DENIED**.

I. Background

A. Factual Background

Petitioners are the parents of A.K. Pet. for Compensation on Behalf of a Minor ("Pet.") at 1, ECF No. 1. Like many children his age, eight-year-old A.K. received two doses of the

[1] This Opinion was initially filed on October 27, 2022, and the parties were afforded fourteen days to propose redactions. The parties did not. Thus, this Opinion is reissued in its original form for publication.

FluMist vaccine in the autumn of 2014. *Id.* ¶¶ 2–4. However, unlike his peers, A.K. began to show signs of heightened fatigue one month after his second dose. *Id.* ¶ 5.

Over the next eighteen months, Petitioners sought medical care from several physicians, starting with their pediatrician, to whom they returned six times in one year. Dec. at 2–3, ECF No. 74 (April 13, 2015; April 21, 2015; May 4, 2015; December 17, 2015; December 29, 2015; March 10, 2016). Meanwhile, A.K.'s symptoms worsened. What began as a disturbing combination of fatigue, poor sleep, and irritability progressed into episodic weariness, chronic malaise, depression, abdominal pain, and the sudden loss of muscle tone. Pet. ¶¶ 5–6, 8–10; Pet.'s Ex. 4 at 6, ECF No. 7-5. Triggered by laughter, A.K.'s buccofacial muscles would involuntarily relax: his eyes would roll into the back of his head and his face would droop "as if he were drunk." Pet.'s Ex. 2 at 2, ECF No. 7-3.

In December 2015, after a series of unsuccessful diagnostic attempts, A.K.'s pediatrician ordered an antinuclear antibody test.[2] *Id.* ¶ 12; Dec. at 3. The presence of antinuclear antibodies in A.K.'s blood raised a red flag, so in March 2016, his pediatrician referred him to a neurologist. Pet. ¶ 13; Dec. at 3. Dissatisfied with a five-month wait time for nearby neurologists, the Kalajdzics traveled over 400 miles to the Children's Hospital of Colorado. Pet. ¶ 14. Between late May and early June 2016, A.K. underwent a series of studies. *Id.* ¶¶ 15–16. This time, the results were conclusive. On June 5, 2016, doctors diagnosed nine-year-old A.K. with narcolepsy and cataplexy. *Id.* ¶ 16.

Narcolepsy is a neurological disorder affecting the ability to regulate wakefulness. Pet.'s Ex. 16 ("Hughes Rep.") at 6, ECF No. 31-2. In a non-narcoleptic brain, neurons located in the lateral hypothalamus produce hypocretin, "a neurotransmitter with complex roles in regulating sleep." *Id.* Depletion of hypothalamic hypocretin neurons—the main function by which narcolepsy affects the brain—can have a drastic impact on the ability to control the sleep-wake cycle. *Id.* Often, narcolepsy manifests in a sudden loss of muscle tone, known as cataplexy. *See* T. Scammell, *Narcolepsy*, 373 N. Engl. J. Med. 2654, 2654–55 (2015), Pet.'s Ex. 25 ("Scammell"), ECF No. 32-1. During cataplectic episodes, individuals are awake but either fully or partially paralyzed. *Id.* at 2654. These episodes are triggered by strong positive emotions, such as laughter. *Id.* Unfortunately, cataplectic symptoms frequently signal an irreversible loss of hypocretin. National Institute of Neurological Disorders and Stroke, *Narcolepsy Fact Sheet*, NIH Publication No. 17-1637, (last visited Oct. 27, 2022), https://www.ninds.nih.gov/narcolepsy-fact-sheet#3201_7. Although some of the symptoms are treatable, there is no known cure for narcolepsy. *Id.*

[2] Antinuclear antibodies attack ("ANA") cellular nuclei. Normally, the body produces antibodies to fight foreign infections. A positive ANA test indicates that the immune system has launched an autoimmune reaction against one's own tissues. Mayo Clinic, *ANA Test*, (last visited Oct. 27, 2022), https://www.mayoclinic.org/tests-procedures/ana-test/about/pac-20385204.

When the Kalajdzics filed their Petition for Compensation on Behalf of a Minor, A.K. was still suffering from narcolepsy with cataplexy.[3] Pet. ¶ 17. His present health status is unknown.

B. Proceedings Before the Chief Special Master

On June 13, 2017, the Kalajdzics filed a petition under the Vaccine Act. *See* Pet. Their original petition alleged the FluMist vaccine caused A.K. to develop narcolepsy. *See id.* ¶ 18. In March 2018, after Petitioners filed the pertinent medical records, the Secretary of Health and Human Services ("Respondent") recommended against compensation pursuant to Vaccine Rule 4(c). *See* Statement of Completion, ECF No. 29; Resp't's Rule 4(c) Rep. ("Resp't's Rep.") at 8, ECF No. 16; Dec. at 20. In its report, Respondent contended that Petitioners were not entitled to compensation due to A.K.'s belated onset of narcolepsy symptoms and simultaneous infection with the phenotypically similar Epstein-Barr virus. Resp't's Rep. at 2, 6–7.

On August 20, 2021, Petitioners moved for a ruling on the record based on preponderant evidence that FluMist can trigger narcolepsy and did so in the case of A.K. within a clinically accepted timeframe. *See* Mot. for Ruling on the Rec., ECF No. 70; Memo in Support of Mot. for Ruling on the Rec., ECF No. 70-1. The Government responded on October 26, 2021, discounting Petitioners' first two claims and conceding the third. *See* Resp. to Mot. for Ruling on the Record, ECF No. 72.

Petitioners' Reply focused on a dispute over the "proper scientific methodology and the level of scientific certainty necessary to 'tip the balance' on vaccine causation." Reply in Supp. of Mot. for Ruling on the Record ("Reply") at 2, ECF No. 73. When a Government expert offers an alternative medical or scientific theory, a special master may make "requisite findings of fact and conclusions of law" to grapple with their competing explanations. *Id.* (citing Vaccine Rule 3(b)(1)). Respondent offered no such theory. *Id.* In the absence of competing theories, Petitioners argued there were no "requisite" findings of fact. *Id.* at 3. According to the Kalajdzics, when the parties agree on the facts, the special master's task is limited to making conclusions of law, i.e., "whether [Petitioners] have met their legal burden under *Althen*." *Id.*; *see Althen v. Sec'y of Health & Hum. Servs.*, 418 F.3d 1274 (Fed. Cir. 2005). Petitioners averred that Respondent raised the burden by going beyond a reliability determination under *Daubert*. Reply at 4 (citing *Daubert v. Merrell Dow Pharms., Inc*, 509 U.S. 579, 593–94 (1993)), 5 (citing *Terran v. Sec'y of Health & Hum. Servs.*, 195 F.3d 1302, 1316 (Fed. Cir. 1999)). Their approach to *Daubert* also precluded special masters from assessing expert reports for credibility other than

[3] The above factual summary addresses only part of a tragic medical record. Narcolepsy with cataplexy presents a pernicious pathology. Its symptoms wreak havoc on young lives and, regularly, go undiagnosed. *See, e.g.*, Sona Nevsimalova, *Narcolepsy in Childhood*, 13(2) Sleep Med Rev. 169 (2009) ("Pediatric cases of narcolepsy are among the most often under recognized and underdiagnosed diseases."). Mr. and Mrs. Kalajdzic turned over every stone to find care for their child. Their persistence in that regard is worthy of note.

a simple background and experience check. *Id.* In part, these arguments reappear in Petitioners' pending motion.

1. Expert Opinions

Both parties submitted expert reports. Petitioners' first expert was Dr. Benjamin Hughes, a board-certified pediatrician with experience in sleep medicine. *See* Pet.'s Ex. 17, ECF No. 31-3. He opined that the FluMist vaccination most likely caused narcolepsy in A.K. *See* Hughes Rep. at 1. Petitioners' second expert was Dr. S. Sohail Ahmed, a specialist in immunology, rheumatology, and vaccine development. *See* Pet.'s Ex. 31, ECF No. 47-2. His report hypothesized a link between FluMist and the early onset of narcolepsy. Pet.'s Ex. 30 ("Ahmed Rep.") at 1, ECF No. 47-1.

The Government responded with one expert, Dr. Thomas J. Dye, a board-certified child neurologist with training in neurologically based sleep disorders. *See* Resp't's Ex. B, ECF No. 36-19. Dr. Dye disputed Petitioners' evidence linking FluMist to narcolepsy. *See* Resp't's Ex. A ("Dye Rep.") at 6, ECF No. 36-1. In rebuttal, Petitioners submitted a supplemental report from Dr. Ahmed in which he criticized Dr. Dye's narrow approach to epidemiological evidence. *See* Pet.'s Ex. 43 ("Ahmed Supp."), ECF No. 65-1. He then reiterated, at length, his causation hypothesis. *See id.* Dr. Dye submitted a supplemental report to refute Dr. Ahmed's primary arguments and bolster his own research on narcolepsy. *See* Resp't's Ex. C ("Dye Supp."), ECF No. 58-1.

a. Dr. Hughes's Report

Petitioners' expert, Dr. Hughes, concluded "to a reasonable degree of medical probability, [that] the FluMist [vaccines] received by A.K. were a substantial factor in the causation of his onset of narcolepsy." Hughes Rep. at 7. His analysis, in part, reviewed literature on narcolepsy pathogenesis and the biologic plausibility of causation. *See id.* at 4–7. Dr. Hughes's medical literature review revealed "numerous cases of narcolepsy . . . onset following H1N1 influenza infection or immunization." *Id.* at 6. While he acknowledged these cases were linked to Pandemrix, a different vaccine, he presented evidence that influenza infections and other influenza vaccines can also trigger narcolepsy. *Id.*

Dr. Hughes's report relied on two studies which demonstrated the mechanism by which upper airway infections might cause narcolepsy. *See id.* 6–7 (first citing Scammell, 373 N. Engl. J. Med. at 2657, to explain a natural infection's destruction of hypothalamic hypocretin neurons and then citing Guo Luo, et al., *Autoimmunity to Hypocretin and Molecular Mimicry to Flu in Type 1 Narcolepsy*, 115(52) Proc. Natl. Acad. Sci. USA E12323, E12323-32 (2018), to show how H1N1 antigens in vaccines might mimic the autoimmune response of a natural infection). Because FluMist stimulates an immune response against four different antigens, including H1N1, Dr. Hughes inferred a "causative role of H1N1 infection or immunization" in cases of narcolepsy pathogenesis. *Id.* at 7. The temporal relationship, the "abundance of similar cases" in medical literature, and his understanding of narcolepsy convinced Dr. Hughes to a "reasonable degree of medical probability" that FluMist can cause narcolepsy and did so in A.K.'s case. *Id.*

b. Dr. Ahmed's Report

Like Dr. Hughes, Dr. Ahmed also tried to establish disease-causation. Definitive causation evades pathologists because "vaccines induce disease in a limited number of genetically susceptible hosts (weakening the power of epidemiological studies to detect a signal) and because each vaccine component can induce autoimmunity triggered through one of several mechanisms." Ahmed Rep. at 6. Put simply, vaccine-induced disease is often too rare to study and too complex to isolate.

Dr. Ahmed then noted that "[m]ultiple reliable, independent epidemiology and molecular mechanistic studies support that infections, including the 2009 H1N1 pandemic influenza strain, can trigger early onset of narcolepsy in a genetically susceptible child."[4] *Id.* at 4. Those studies suggest that the same is likely true of certain vaccine formulations, specifically live attenuated influenza vaccines ("LAIVs") like FluMist.[5] *See id.* at 6–7.

Although FluMist's viral strains are "attenuated with reduced ability to cause an influenza-like respiratory infection," Dr. Ahmed theorized an autoimmunological response to FluMist that would mirror an influenza infection.[6] *Id.* at 7. So, his argument goes, evidence linking influenza infection to narcolepsy could double as evidence linking LAIVs to narcolepsy. Because the Vaccine Act does not compensate the former, Petitioners' task is to explain A.K.'s narcolepsy pathogenesis via the latter.

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[4] These studies include M. Bonvalet, et al., *Autoimmunity in Narcolepsy*, 23(6) Current Opinion in Pulmonary Medicine 522 (2017), and C. Siegrist, et al., *Meeting Report Narcolepsy and Pandemic Influenza Vaccination: What We Know and What We Need to Know Before the Next Pandemic? A Report from the 2nd IABS Meeting*, 41(3) Drug Safety, 537 (2018).

[5] Live attenuated influenza vaccines ("LAIVs") use weakened forms of the disease-causing virus. U.S. Dep. of Health & Hum. Servs., *Vaccine Types*, (last visited Oct. 27, 2022), www.hhs.gov/immunization/basics/types/index.html. Some vaccines contain only "killed"—not weakened—versions of the virus. *Id.* These "inactivated vaccines" provide less immunity but are also less likely to infect recipients with weak immune systems. *Id.* Patients with weakened immune systems are at higher risk for infection because live attenuated viral vaccines contain a small amount of the live virus. *Id.*

[6] One such mechanism is molecular mimicry. Ahmed Rep. at 7 (citing I. Shannon, et al., *Understanding Immunity in Children Vaccinated with Live Attenuated Influenza Vaccine*. 9(1) J. Pediatric Infectious Diseases Soc. S10 (2020)). Immune attack cells are activated by the presence of a foreign infectious agent and then mistakenly attack native cells because they have properties similar to the foreign infectious agent. *See generally* Manuel Rojas, et al., *Molecular Mimicry and Autoimmunity*, 95 J. Autoimmunity 100 (2018).

Dr. Ahmed attempted to do exactly that. He claimed influenza infection alone is unlikely to explain A.K.'s case. *Id.* First, the natural "[o]nset of narcolepsy before age ten is rare." *Id.* Here, A.K. was only eight years old when he first exhibited symptoms. *Id.* Additionally, "[t]he double dose of the live-attenuated FluMist vaccine increased A.K.'s risk that an already ongoing autoimmune process to his first influenza vaccine would be boosted by the second." *Id.* at 8. The "dual administration" of the vaccine distinguishes this case from others. *Id.* at 11. The report described how the administration might create the "rare circumstance of increased risk specifically in A.K." because of his genetic predisposition to narcolepsy. *Id*. Essentially, Dr. Ahmed believed the second dose compounded the chance that, if it were not already occurring, the vaccine would catalyze an adverse reaction. *Id.* at 8. For these reasons, Dr. Ahmed thought FluMist likely contributed to the development of narcolepsy in A.K.

c. Dr. Dye's Report

In contrast, Dr. Dye negated the theory linking FluMist to A.K.'s narcolepsy. Dye Rep. at 5 ("[N]o cases of narcolepsy have been linked to the FluMist vaccine."). To rebut Dr. Ahmed's argument on its own terms, Dr. Dye's report first applied datasets from the Pandemrix studies. *Id.* Even if there were a causal relationship between FluMist and narcolepsy, the "timing of symptom onset following Pandemrix vaccination . . . would be somewhat inconsistent with the symptom onset reported in [A.K.'s] case." *Id.* Following Pandemrix vaccination, the mean time to symptom onset was 53.8 days with a 95% confidence interval of onset between 40 and 67 days. *Id.* His report ranked the "likelihood of narcolepsy symptoms being present" during A.K.'s visit to his pediatrician. *Id.* at 4 ("4/13/2015, *potentially*, 9/10/2015, *likely*, 12/15/2015, *certainly*. This would signify symptom onset to have likely occurred in late spring or summer of 2015."). According to Dr. Dye, A.K.'s timeline departs from the medical community's only known timeline for post-vaccine narcolepsy pathogenesis. *Id.* at 4–5.

It conforms, however, with the timeline for natural histories of narcolepsy. Generally, narcolepsy symptoms emerge "during the late spring and summer, peaking between . . . April and July." *Id.* at 4 (citing F. Han, et al., *Decreased Incidence of Childhood Narcolepsy Two Years After The 2009 H1N1 Winter Flu Pandemic*, 73(4) Ann. Neurol. 560 73 (2013)). A.K.'s relevant medical record begins on April 13, 2015. *See* Pet.'s Ex. 3 at 6, ECF No. 7-4 (High Desert Pediatrics records). Additionally, children born in March are more likely to develop narcolepsy based on the season during which the symptom first presents. Dye Rep. at 4–5. A.K. was born on March 16, 2006. *E.g.*, Pet.'s Ex. 2 at 1 ECF No. 7-3 (Children's Hospital of Colorado records). These facts point to a "natural history of narcolepsy rather than . . . an unusual presentation specifically correlated with vaccine administration." Dye Rep. at 5.

Dr. Dye's second relevant contention concerned the efficacy of the FluMist vaccination. *Id.* There is "some question" whether the 2013–2014 and 2015–2016 batches of FluMist "elicit[ed] an appropriate immune response . . . to protect against H1N1." *Id.* at 5–6. If true, this would undermine Dr. Ahmed's central contention. As characterized by Respondent, the Petitioners' proposed mechanism for vaccine-induced narcolepsy requires an effective strain of H1N1 to destroy hypothalamic hypocretin neurons. *Id.* But Dr. Dye contends "it is unlikely that [A.K.] received an effective exposure to H1N1 from the FluMist vaccine. Therefore, the suggestion that exposure to H1N1 from the FluMist vaccine resulted in his narcolepsy is highly dubious." *Id.*

d. Supplemental Expert Reports

Dr. Ahmed submitted a supplemental report. *See* Ahmed Supp. His second filing "repeated many prior arguments instead of adding detail to existing ones." Dec. at 11 n.10. He reiterated the epidemiological evidence for an association between influenza infections and the early onset of narcolepsy in children, especially within six months post-infection. Ahmed Supp. at 2. He again wrote that failure of epidemiological studies to demonstrate statistical significance "does not preclude biological plausibility." *Id*. at 6. "Failure to find an increased risk [of vaccine-induced disease] does not equate to zero individual causation risk. *Id.* at 6. Vaccine cases examine statistically rare pathogeneses—for instance, whether A.K. is "one of these rare individuals that compelling science and clinical studies tells us can, albeit rarely, [develop disease] after vaccination." *Id.* Thus, the dearth of documented links between FluMist and narcolepsy is both expected and not dispositive.

Furthermore, Dr. Ahmed questioned whether Dr. Dye's point about the inefficacy of the 2013–2014 and 2015–2016 FluMist vaccines to trigger immunity is equally applicable to the link between FluMist and narcolepsy. *Id.* at 7–8. While the relevant batch of FluMist was ineffective against H1N1, Dr. Ahmed argued another influenza strain (H3N2) against which FluMist was effective "trigger[ed] the same immune response as the H1N1 leading to narcolepsy." *Id.* at 8. Finally, Dr. Ahmed defended against Dr. Dye's claim that there were no documented cases of FluMist causing narcolepsy. *Id.* at 10–14 (citing two such cases documented in the Vaccine Adverse Event Reporting System).

Dr. Dye's supplemental report presented three rebuttals. First, he rejected Dr. Ahmed's claim that A.K. was younger than expected for narcolepsy patients. Dye Supp. at 1–2 (presenting a more recent study in favor of the natural history timeline preferred by Dr. Dye). Then, he took issue with Petitioners' emphasis on dual administration. *Id.* at 2–4. A significant percentage of genetically predisposed children who received a two-dose regimen never developed narcolepsy. *Id.* He also reasserted his prior claims on the inefficacy of the relevant FluMist batches. *Id.* at 4.

2. The Chief Special Master's Decision Denying Compensation

The Chief Special Master dismissed the Kalajdzics' Petition on June 17, 2022. *See* Dec. First, the decision classified the Petition as an off-table case. *Id.* at 23. Under the Vaccine Act, a petitioner must prove either: "(1) that he suffered a [t]able [i]njury—i.e., an injury falling within the Vaccine Injury Table—corresponding to one of the vaccinations in question within a statutorily prescribed period of time or, in the alternative, (2) that his illnesses were actually caused by a vaccine ([an off-table injury])." *Id*. (internal quotations omitted). Narcolepsy is not an injury covered by the Vaccine Act for seasonal influenza vaccines. *Id.* Thus, the burden is on the Petitioners to prove actual causation.

a. Petitioners did not establish the *Althen* prongs by a preponderance of the evidence.

Once the case was categorized off-table, the Chief Special Master rejected Petitioners' claim because they failed to meet their evidentiary burden. *See id*. at 32. To succeed on an off-table claim, petitioners must show:

> (1) a medical theory causally connecting the vaccination and the injury; (2) a logical sequence of cause and effect showing that the vaccination was the reason for the injury; and (3) a showing of a proximate temporal relationship between vaccination and injury.

Althen v. Sec'y of Health & Hum. Servs., 418 F.3d 1274, 1278 (Fed. Cir. 2005); *see also* Dec. at 24. Vaccine Program petitioners must prove these elements by a "preponderance of the evidence." *E.g.*, 42 U.S.C. §§ 300aa-13(a); *Althen*, 418 F.3d at 1279. Evidence that leads the "trier of fact to believe that the existence of a fact is more probable than its nonexistence" satisfies this burden. *Moberly*, 592 F.3d at 1322 n.2.

While Respondent conceded the third *Althen* prong, the parties extensively briefed the first and second prongs. Ultimately, the Chief Special Master found Petitioners did not prove a causal relationship between FluMist and narcolepsy. Dec. at 31–33. Nor did they prove a logical sequence of cause and effect between A.K.'s Fall 2015 inoculations and the onset of disease. The Chief Special Master could have ended his analysis after Petitioners' failure to prove a causal link. *Id.* at 34. Nonetheless, his decision addressed all three prongs.

i. Petitioners failed under the first *Althen* prong.

Prong one of *Althen* focuses on whether a vaccine "*can cause* the type of injury alleged." *Id*. The Chief Special Master noted the absence of a reliable link between FluMist and narcolepsy. *See id.* at 31. The same was true in *D'Tiole v. Sec'y of Health & Human Servs.* No. 15-085V, 2016 WL 7664475 (Fed. Cl. Spec. Mstr. Nov. 28, 2016). There, the petitioner made nearly identical allegations about narcolepsy and FluMist. *See id.*; Dec. at 31. The *D'Tiole* petitioner attempted to transfer the Pandemrix theory onto a case involving FluMist, "but [did not show] that the theory is similarly reliable in the different setting." *D'Tiole*, 2016 WL 7664475 at *20.

Petitioners relied on the studies previously presented to the Chief Special Master in *D'Tiole.* One such study linked narcolepsy to Pandemrix. But Pandemrix is not FluMist; Pandemrix was an intramuscular and inactivated vaccine containing only one H1N1-like virus. It also contained adjuvants, which are vaccine ingredients used to create a stronger immune response in vaccine recipients. Center for Disease Control and Prevention, *Adjuvants and Vaccines*, (last visited Oct. 27, 2022), www.cdc.gov/vaccinesafety/concerns/adjuvants.html.

FluMist was different in four ways: it was intranasal, nonadjuvanted, quadrivalent, and live-attenuated. *See generally* Dye Rep.; Dye Supp. The quadrivalent version of FluMist protects against four different flu viruses. U.S. Food and Drug Admin., *FDA Information Regarding FluMist Vaccine Quadrivalent Vaccine* (published Jan. 26, 2018). While both

Pandemrix and FluMist contained an A(H1N1)pdm09 strain ("2009 strain"), the FDA concluded that the version of the strain included in FluMist 2013–2014 (A/California/07/2009) was ineffective due to problems with "thermostability," i.e., the ability of a vaccine to resist irreversible chemical changes with elevations in temperature. *Id*. The same was true of the version included in FluMist 2015–2016 (A/Bolivia/559/2013). Dye Rep. at 5.

Dr. Dye reasoned that (1) if the 2009 strain is the only strain confirmed to deplete hypothalamic hypocretin neurons and (2) if FluMist contained ineffective versions of this strain, then (3) FluMist did not contain effective versions of the sole strain confirmed to deplete hypothalamic hypocretin neurons. *See* Dye Supp. at 4. Dr. Ahmed's theory on how Pandemrix interferes with hypocretin neurons was persuasive, but exclusive to Pandemrix. The Chief Special Master decided that Dr. Ahmed's theory was too specific to Pandemrix and that his expert report did nothing to address this concern. Dec. at 31.

Instead, the decision below relied on several meta-studies presented by Dr. Dye. (Meta-studies collect and analyze multiple studies with the same or similar research question.) One meta-study suggested that "a FluMist-narcolepsy association has [not] become any more likely than it was [five years ago]." *Id.* at 32. Importantly, numerous "larger scale studies found no association between narcolepsy and any *non-adjuvanted* versions of the flu vaccine," like FluMist. Dec. at 17 (citing T. Sarkanen et al., *Incidence of Narcolepsy After H1N1 Influenza and Vaccinations: Systemic Review and Meta-Analysis*, 38 Sleep Med. Rws. 177 (2018) ("Sarkanen")). Petitioners' experts made no mention of these studies.

Sarkanen considered every published study on the topic through 2015. In sum, those studies revealed "no elevated risk for narcolepsy associated with any vaccine other than Pandemrix." Dec. at 17. While Sarkanen cites Dr. Ahmed's findings about the possible mechanisms by which an influenza vaccine could cause narcolepsy, the meta-study notes that Dr. Ahmed's work "remains controversial." Sarkanen at 184. If A.K. had been vaccinated with Pandemrix, Petitioners' effort to prove a causal link would have been far easier. FluMist, however, remains just as unlikely to cause narcolepsy as it was six years ago in *D'Tiole.*

Another notable study surveyed 650,995 individuals vaccinated against the 2009 strain and another 870,530 who received multivalent, seasonal vaccines. Dec. at 17 (citing J. Duffy et al., *Narcolepsy and Influenza A (H1N1) Pandemic 2009 Vaccination in the United States*, 83 Neurology 1823 (2014) ("Duffy")). Despite expecting around seven participants to develop narcolepsy, researchers observed zero such cases. *Id.* In the same study analyzing the 2010–2011 flu season, the expectation was that around nine participants would develop narcolepsy. *Id.* Only two did. *Id.* at 17 (citing Duffy at 1827). Additionally, out of the 45,246 participants who received a LAIV, none developed narcolepsy. *Id.* The study concluded that the H1N1 strain "could not be associated with an increased risk of narcolepsy." *Id.* (citing Duffy at 1823).

Contrary to Petitioners' argument, the Chief Special Master specifically noted that his conclusion "[did] not reflect a mistaken substitution of a standard of scientific certainty in place of . . . preponderance." *Id.* at 33. The "overall chain of contentions that constitute[d] the Petitioner[s'] theory ha[d] too many omissions and gaps to conclude 'more likely than not' that FluMist can cause narcolepsy." *Id.* "It is thus . . . *unlikely* that FluMist can cause narcolepsy." *Id.* His rejection sounded in preponderance, not certainty.

ii. Petitioners failed under the second *Althen* prong.

To satisfy the second prong, Petitioners had to demonstrate a logical sequence of cause-and-effect between narcolepsy and FluMist. *Id.* at 25. *Althen* invites petitioners to anchor their petition in facts-at-hand and shift the inquiry from paper to patient. Usually, petitioners prove the second prong with facts from the patient's medical record. *Id.* (citing *Cucuras v. Sec'y of Health & Hum. Servs*., 993 F.2d 1525, 1528 (Fed. Cir. 1993)). Such facts imbue a heightened trustworthiness compared to post-hoc records or evidence. *Id.*

Petitioners focused on one fact in particular from the medical record: both parties agreed that A.K. possessed a genetic predisposition for narcolepsy. *Id.* at 34. But the Chief Special Master agreed with Respondent. Genetic predisposition is a risk factor "associated with narcolepsy generally—not one associated with vaccination as the specific trigger." *Id.* Indeed, many similarly situated children with the same genetic predisposition, who received the FluMist vaccine during the same timeframe as A.K., never developed narcolepsy. *Id.*

Other than A.K.'s genetic predisposition, Petitioners did not point to any discussions between themselves and A.K.'s physicians about a possible link between narcolepsy and FluMist. In fact, A.K.'s physicians seemingly never wrestled with etiological questions, i.e., *what caused his conditions. Id.* Instead, they predominantly sought answers to pathological questions, i.e., *what conditions A.K. might have*. *Id.* The record reflects a substantial lack of contemporaneous discussion about FluMist as a potential cause. Notably, A.K.'s pediatrician did not submit a report in support of Petitioners' claim. Post-hoc expert conjecture on etiology is not an adequate substitute for contemporaneous medical records. As such, the record did not "include sufficient evidence that would permit [the Chief Special Master] to find that the FluMist vaccine likely *did cause* A.K. to experience narcolepsy." *Id.* Thus, Petitioners also fell short of *Althen*'s second pleading requirement.

iii. Respondents conceded the third *Althen* prong.

To satisfy the third prong, petitioners must preponderantly prove that symptoms began within a medically accepted timeframe. *Id.* at 25 (citing *de Bazan v. Sec'y of Health & Hum. Servs.*, 539 F.3d 1347, 1352 (Fed. Cir. 2008)). In other words, given what the medical community knows about narcolepsy, did A.K.'s symptoms begin soon enough after inoculation to infer causation? Respondents did not rebut—and therefore conceded—Petitioners' claims under the third prong. *Id*. at 34.

For failure to prove preponderantly the first and second prongs of *Althen*, the Chief Special Master denied compensation. One month after the entitlement decision, Petitioners moved for review in this Court. Pet.'s Mot. for Rev. of Dec. ("Mot. for Rev."), ECF No. 76.

II. Jurisdiction

This Court has jurisdiction to review a Vaccine Act case upon a motion from the petitioner. 42 U.S.C. § 300aa–12(e)(2). Three standards guide review. Findings of fact are reviewed under the arbitrary and capricious standard; questions of law are reviewed under the not in accordance with law standard; and discretionary rulings are reviewed under the abuse of

discretion standard. *Masias v. Sec'y of Health & Hum. Servs.*, 634 F.3d 1283, 1287–88 (Fed. Cir. 2011); *Munn v. Sec'y of Health & Hum. Servs.*, 970 F.2d 863, 870 n.10 (Fed. Cir. 1992); *see* 42 U.S.C § 300aa–12(e)(2)(B). Only the second is relevant, because Petitioners pose a question of law. *See Althen*, 418 F.3d at 1277–78.

III. The Chief Special Master Applied the Appropriate Burden of Proof.

This Court reviews whether the Chief Special Master's application of the *Daubert* factors constitutes clear legal error. The Kalajdzics request an answer in the affirmative. They contend the "Chief Special Master's application of the *Daubert* factors undermine[d] *Althen*," and was not in accordance with law. Mot. for Rev. at 7. The Government asks this Court to affirm the decision below. Resp't's Resp. to Mot. for Rev. ("Resp't's Resp.") at 1, ECF No. 78. It points to this Court's highly deferential standard of review and argues the Chief Special Master's conclusions were based on a sufficiently "thorough review of the evidence." *Id.* at 8.

Normally, judges apply *Daubert* to shield juries from unreliable or confusing evidence. 509 U.S. at 593–94. Judges weigh four factors from *Daubert*: (1) whether a theory or technique can be and has been tested; (2) whether the theory or technique has been subjected to peer review and publication; (3) whether there is a known or potential rate of error and whether there are standards for controlling the error; and (4) whether the theory or technique enjoys general acceptance within a relevant scientific community. *Id*. In the Vaccine Program, special masters serve as both evidentiary gatekeepers and factfinders. Rather than use *Daubert* to exclude unreliable or confusing evidence, special masters may use the *Daubert* factors to weigh the reliability of the scientific evidence proffered. *Davis v. Sec'y of Health & Hum. Servs.*, 94 Fed. Cl. 53, 66–67 (2010).

The issue on appeal is how to apply the *Daubert* factors. Petitioners believe the four questions in *Daubert* are the only "indicia of reliability" with which a special master may consider the weight of expert testimony. Mot. for Rev. at 7 (citing *Cedillo v. Sec'y of Health & Hum. Servs.*, 617 F.3d 1328, 1329 (Fed. Cir. 2010)). While they acknowledge circumstances under which a special master may "examine expert witness testimony for credibility," they argue credibility should be limited to "an expert's background and experience." *Id.* at 8 (citing *LaLonde v. Sec'y of Health & Hum. Servs.*, 746 F.3d 1334, 1342 (Fed. Cir. 2014) (Newman, J., dissenting)).

Petitioners assert the Chief Special Master "review[ed] the medical testimony and medical literature through the lens of a laboratorian, [made] conclusions on the persuasiveness and believability of the Respondent's expert testimony[, and] reject[ed] the Petitioners' expert testimony . . . as unreliable and unpersuasive." Mot. for Rev. at 13 (internal quotations omitted).

Certainly, Petitioners are correct that the Chief Special Master went beyond the indicia of reliability in *Daubert*. *Id.* Examples abound. He considered the "relative persuasiveness of [the competing experts'] theories." Dec. at 28. In returning to his analysis in *D'Tiole*, he again examined the "scientific reliability and evidentiary persuasiveness" of the FluMist-narcolepsy link. *Id.* at 30. His decision did not find the Vaccine Adverse Event Reporting System to be "especially probative." *Id.* at 32. Throughout his decision, he judged the experts' reports based

on reliability standards untethered to *Daubert*. While Petitioners think this practice is contrary to law, Respondent stands by the more flexible approach to reliability employed by special masters.

One example in particular elucidates the parties' disagreement. Drs. Ahmed and Dye disagreed on whether "any vaccine containing some form of H1N1 . . . virus strain would have the propensity to cause narcolepsy." Dec. at 11 (emphasis removed). They agreed, however, on all relevant facts: (1) A.K. is genetically predisposed to narcolepsy; and (2) one version of the H1N1 flu virus can erode hypothalamic hypocretin neurons to cause narcolepsy. *Id.* at 16, 19. Keeping with the example, Petitioners allege the Chief Special Master's task is to apply *Daubert* to the expert testimony underpinning those two facts. Mot. for Rev. at 13–16. Assuming the facts pass muster under *Daubert,* the next and final step in Petitioners' framework is to analyze whether Petitioners' conclusion comports with the *Althen* pleading standards. *Id.* at 16–17 ("[The] sole [remaining] legal question . . . is whether Petitioners' causation-in-fact vaccine theory, not expert testimony and medical literature, is legally probable under the 'vantage point of the [Vaccine] Act's preponderance standard' clearly enunciated in *Althen*, 418 F.3d at 1280.").

The Government correctly places less emphasis on *Daubert*. Those factors are merely a guide to determine reliability. Resp't's Resp. at 4. Special masters are free to "fashion standards of reliability other than those suggested in *Daubert*," if those standards are reasonable. *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999). The Federal Circuit affords great deference to special masters in choosing how to ascertain reliability. *See Lampe v. Sec'y of Health & Hum. Servs.*, 219 F.3d 1357, 1361–62 (Fed. Cir. 2000) (upholding the special master's determination that the respondent's medical expert was more persuasive than the petitioners' medical expert because "[t]hose findings . . . are largely based on [the special master's] assessments of the credibility of the witnesses and the relative persuasiveness of the competing medical theories of the case. As such, they are virtually unchallengeable on appeal."); *de Bazan*, 539 F.3d at 1354 (upholding the special master's determination that respondent's expert testimony was more credible and probative than that of the petitioner's expert); *Broekelschen v. Sec'y of Health & Hum. Servs.*, 618 F.3d 1339, 1347 (Fed. Cir. 2010) (permitting the credibility of experts and persuasiveness of their competing theories to factor into special masters' decisions); *Hodges v. Sec'y of Health & Hum. Servs.*, 9 F.3d 958, 961 (Fed. Cir. 1993) (describing the "uniquely deferential" posture of Vaccine Act appeals).

As such, the disposition of this case is clear. It would be wrong to construe the decision below as applying *Daubert* contrary to the law as it currently stands. Notwithstanding Petitioners' suggestions, this Court may not "reweigh the factual evidence, . . . assess whether the special master correctly evaluated the evidence[, or] examine the probative value of the evidence or the credibility of the witnesses." *Id.* (quoting *Munn*, 970 F.2d at 871). If the Chief Special Master "considered the relevant evidence of record, [drew] plausible inferences and articulated a rational basis for the decision," reversal may seem like a Sisyphean burden. *Hines v. Sec'y of Health & Hum. Servs.*, 940 F.2d 1518, 1528 (Fed. Cir. 1991) (holding that "reversible error is extremely difficult to establish."). The Chief Special Master considered all the relevant evidence of record, drew plausible inferences, and articulated a rational basis for his decision. The decision was in accordance with law.

IV. Conclusion

The Court is not unsympathetic to the Kalajdzics. However, for the reasons set forth above, Petitioners' Motion for Review is **DENIED**. The Clerk is directed to enter judgment accordingly.

IT IS SO ORDERED.

s/ Carolyn N. Lerner
CAROLYN N. LERNER
Judge